

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 2

agent wherein; the synergistic therapeutic effect is the treatment of cancers of the brain, breast, colon, genitourinary tract, lymphatic system, pancreas, rectum, stomach, larynx, liver, lung, prostate, stet histiocytic lymphoma lung adenocarcinoma, pancreatic carcinoma, colo-rectal carcinoma, small cell lung cancers or neurological tumor cancer whose growth is inhibited by the administration of the prenyl-protein transferase inhibitor and the antineoplastic agent.

50. (New) The method according to Claim 49 wherein an amount of a prenyl-protein transferase inhibitor and an amount of a microtubule-stabilizing agent are administered simultaneously.

51. (New) The method according to Claim 49 wherein an amount of a microtubule-stabilizing agent and an amount of a prenyl-protein transferase inhibitor are administered consecutively.

52. (New) The method according to Claim 49 wherein the antineoplastic agent is selected from: paclitaxel, epothilone A, epothilone B, desoxyepothilone A or desoxyepothilone B.

53. (New) A method for achieving a synergistic therapeutic effect in a mammal in need thereof which comprises administering to said mammal amounts of at least two therapeutic agents selected from a group consisting of:

- a) a prenyl-protein transferase inhibitor and
- b) an antineoplastic agent selected from paclitaxel, epothilone A, epothilone B, desoxyepothilone A or desoxyepothilone B.

wherein the synergistic therapeutic effect is the treatment of cancers of the brain, breast, colon, genitourinary tract, lymphatic system, pancreas, rectum, stomach, larynx, liver, lung, prostate, stet histiocytic lymphoma lung adenocarcinoma, pancreatic carcinoma, colo-rectal carcinoma, small cell lung cancers or neurological tumor cancer whose growth is inhibited

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 3

by the administration of the prenyl-protein transferase inhibitor and the antineoplastic agent.

54. (New) The method according to Claim 53 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-Butyl-1-(2,3-diaminoprop-1-yl)-1-(1-naphthoyl)piperazine;

1-(3-Amino-2-(2-naphthylmethylamino)prop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-{5-[1-(2-naphthylmethyl)]-4,5-dihydroimidazol}methyl-4-(1-naphthoyl)piperazine;

1-[5-(1-Benzylimidazol)methyl]-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-{5-[1-(4-nitrobenzyl)]imidazolylmethyl}-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(3-Acetamidomethylthio-2(R)-aminoprop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[2-(1-imidazolyl)ethyl]sulfonyl-4-(1-naphthoyl)piperazine;

2(R)-Butyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-4-(1-naphthoyl)-1-(3-pyridylmethyl)piperazine;

1-2(S)-butyl-(2(R)-(4-nitrobenzyl)amino-3-hydroxypropyl)-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-hydroxyheptadecyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Benzyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine;

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 4

2(S)-Butyl-1-[(4-imidazolyl)ethyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(4-imidazolyl)methyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]acetyl]-  
4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]ethyl]-4-  
(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-hydroxypropyl)-2(S)-butyl-4-(1-  
naphthoyl)piperazine;

1-(2(R)-Amino-4-hydroxybutyl)-2(S)-butyl-4-(1-  
naphthoyl)piperazine;

1-(2-Amino-3-(2-benzyloxyphenyl)propyl)-2(S)-butyl-4-(1-  
naphthoyl)piperazine;

1-(2-Amino-3-(2-hydroxyphenyl)propyl)-2(S)-butyl-4-(1-  
naphthoyl)piperazine;

1-[3-(4-imidazolyl)propyl]-2(S)-butyl-4-(1-naphthoyl)-  
piperazine;

2(S)-n-Butyl-4-(2,3-dimethylphenyl)-1-(4-imidazolylmethyl)-  
piperazin-5-one;

2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-  
(2,3-dimethylphenyl)piperazin-5-one;

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-  
dimethylphenyl)-2(S)-(2-methoxyethyl)piperazin-5-one;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(1-naphthylmethyl)imidazol-  
5-ylmethyl]-piperazine;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-naphthylmethyl)imidazol-  
5-ylmethyl]-piperazine;

2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-  
naphthoyl)piperazine;

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 5

2(S)-n-Butyl-1-[1-(4-methoxybenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-1-[1-(3-methyl-2-butenyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-1-[1-(4-fluorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethylbenzyl)imidazol-5-ylmethyl]-piperazine;

2(S)-n-Butyl-1-[1-(4-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine;

2(S)-n-Butyl-1-[1-(3-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine;

1-[1-(4-Phenylbenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)-piperazine;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-phenylethyl)imidazol-5-ylmethyl]-piperazine;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethoxy)imidazol-5-ylmethyl]piperazine;

1-([1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl)-2(S)-n-butyl-4-(1-naphthoyl)piperazine;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone;

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 6

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-acetamido]-2-piperazinone;

(±)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

5(S)-Butyl-4-[1-(4-cyanobenzyl-2-methyl)-5-imidazolylmethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one;

4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-imidazolylmethyl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)piperazin-2-one;

5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-1-(2-methylphenyl)piperazin-2-one;

4-[1-(4-Cyanobenzyl)-5-imidazolylmethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one;

4-[3-(4-Cyanobenzyl)pyridin-4-yl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)-piperazin-2-one;

4-[5-(4-Cyanobenzyl)-1-imidazolylethyl]-1-(3-chlorophenyl)piperazin-2-one;

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine,

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 7

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylloxy-4-pentenoyl-homoserine lactone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] -  
pentylloxy-4-pentenoyl-homoserine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylloxypentanoyl-homoserine lactone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylloxypentanoyl-homoserine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] 5-  
pentylloxy-4-methylpentanoyl-homoserine lactone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylloxy-4-methylpentanoyl-homoserine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylloxy-3-methylbutanoyl-homoserine lactone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylloxy-3-methylbutanoyl-homoserine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylloxy-3-phenylbutanoyl-homoserine lactone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] -  
pentylloxy-3-phenylbutanoyl-homoserine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine  
lactone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine  
lactone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] -

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 8

pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] -  
pentyloxy-3-phenylpropionyl-methionine methyl ester,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentyloxy-3-phenylpropionyl-methionine,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentyloxy-3-phenylpropionyl-methionine sulfone methyl  
ester,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentyloxy-3-phenylpropionyl-methionine sulfone  
(Compound A),

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] -  
pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl  
ester,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] -  
pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone methyl  
ester,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -methyl] -  
pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone  
methyl ester,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone,

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentyloxy-3-methylbutanoyl-methionine methyl ester.

2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-3(S) -  
methyl]pentyloxy-3-methylbutanoyl-methionine,

Disulphide of 2(S) - [2(S) - [2(R) -Amino-3-mercapto]propylamino-  
3(S) methyl]pentyloxy-3-phenylpropionyl-homoserine lactone,

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 9

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)methyl]pentyloxy-3-methylbutanoyl-methionine methyl ester

1-(4-Biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-5-(4'-phenylbenzamido)ethyl-imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Biphenylethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Bromo-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(3',5'-dichloro)-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Methoxy-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(3',5'-Bis-trifluoromethyl)-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)-4-methylimidazole

1-(4-Biphenylmethyl)-5-(4-cyanophenoxy)-imidazole

5-(4-Cyanophenoxy)-1-(2'-methyl-4-biphenylmethyl)-imidazole



Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 10

5-(4-Biphenyloxy)-1-(4-cyanobenzyl)-imidazole

5-(2'-Methyl-4-biphenoxy)-1-(4-cyanobenzyl)-imidazole

5-(4-(3',5'-dichloro)biphenylmethyl)-1-(4-cyanobenzyl)imidazole

1-(4-biphenylmethyl)-5-(1-(R,S)-acetoxy-1-(4-cyanophenyl)methylimidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-hydroxy-1-(4-cyanophenyl)methylimidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-amino-1-(4-cyanophenyl)methylimidazole

1-(4-biphenylmethyl)-5-(1-(R,S)-methoxy-1-(4-cyanophenyl)methylimidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(4-biphenyl)-methyl imidazole

1-(4-Cyanobenzyl)-5-(1-oxo-1-(4-biphenyl)-methyl imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-fluoro-4-biphenyl)-methyl)-imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-biphenyl)methyl-imidazole

5-(2-[1,1'-Biphenyl]vinylene)-1-(4-cyanobenzyl)imidazole

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

1-(4-Biphenylmethyl)-5-(4-bromophenyloxy)-imidazole

1-(3'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 11

1-(4'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(3'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'3'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'4'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'5'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(3'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'-Fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4-(2'-Trifluoromethylphenyl)-2-Chlorophenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-{1-(4-(2'-trifluoromethylphenyl)phenyl)ethyl}-5-(4-  
cyanobenzyl) imidazole

1-(2'-Trifluoromethyl-4-biphenylpropyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'-N-t-Butoxycarbonylamino-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(2'-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'-Acetylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'-Methylsulfonylamino-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 12

1-(2'-Ethylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'-Phenylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)  
imidazole

1-(2'-Glycinylinomethyl-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(2'-Methyl-4-biphenylmethyl)-2-chloro-5-(4-cyanobenzyl)  
imidazole

1-(2'-Methyl-4-biphenylmethyl)-4-chloro-5-(4-cyanobenzyl)  
imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-4-(4-  
cyanobenzyl) imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-4-(4-  
cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(3'-Methoxy-2-methyl-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(2'-Chloro-4'-fluoro-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-(2-Propyl)-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(2'-(2-Methyl-2-propyl)-4-biphenylmethyl)-5-(4-  
cyanobenzyl) imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-(1H-tetrazol-5-  
yl))benzyl) imidazole

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 13

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethoxy]-4-(2'-methylphenyl)-2-(3-N-phthalimido-1-propyl)benzene

1-(3',5'-Ditrifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3',5'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3',5'-Dimethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-(N-Boc-aminomethyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(3-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-2-methyl-5-(2'-methylbiphenyl-4-yloxy)imidazole

5-(4-Cyanobenzyl)-1-(3-cyano-2'-trifluoromethylbiphenyl-4-ylmethyl)-imidazole

2-Amino-5-(biphenyl-4-ylmethyl)-1-(4-cyanobenzyl)imidazole

2-Amino-1-(biphenyl-4-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Butylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(3-Propylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(4-Biphenylmethyl)-4-(4-cyanobenzyl-2-methylimidazole  
1-(4-Cyanobenzyl)-5-[(3-fluoro-4-biphenyl)methyl]imidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)-1-hydroxy]ethyl-2-methylimidazole

1-(4-Cyanobenzyl)-5-(4-biphenylmethyl)-2-methylimidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]ethyl-2-methylimidazole

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 14

1-(4-Cyanobenzyl-5-[1-(4-biphenyl)]vinylidene-2-methylimidazole and

1-(4-Cyanobenzyl)-5-[2-(4-biphenyl)]vinylene-2-methylimidazole

1-(4-[Pyrid-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-[3-Methylpyrazin-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(Pyrimidinyl-5-yl)phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenylpyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenyl-N-Oxopyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-N-Oxopyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-(3-Trifluoromethoxyphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-(2-Trifluoromethylphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-2-Chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-4-chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Amino-3-phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-[Pyrid-2-yl]pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

N-{1-(4-Cyanobenzyl)-1H-imidazol-5-yl)methyl}-5-(pyrid-2-yl)-2-amino-pyrimidine

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 15

*N,N-bis(4-Imidazolemethyl) amino-3-[(3carboxyphenyl)oxy] benzene*

*N,N-bis(4-Imidazolemethyl) amino-4-[(3carboxyphenyl)oxy] benzene*

*N,N-bis(4-Imidazolemethyl) amino-3-[(3-carbomethoxyphenyl) -  
oxy] benzene*

*N,N-bis(4-Imidazolemethyl) amino-4-[(3-carbomethoxyphenyl) -  
oxy] benzene*

*N-(4-Imidazolemethyl) -N-(4-nitrobenzyl) aminomethyl-3-[(3-  
carboxyphenyl)oxy] benzene*

*N-(4-Imidazolemethyl) -N-(4-nitrobenzyl) aminomethyl-3-[(3-  
carbomethoxyphenyl)oxy] benzene*

*N-(4-Imidazolemethyl) -N-(4-nitrobenzyl) amino-3-  
(phenoxy) benzene*

*N-(4-Imidazolemethyl) -N-(4-nitrobenzyl) amino-4-  
(phenoxy) benzene*

*N-(4-Imidazolemethyl) -N-(4-nitrobenzyl) amino-4-  
(phenylthio) benzene*

*N-Butyl-N-[1-(4-cyanobenzyl)-5-imidazolemethyl] amino-4-  
(phenoxy) benzene*

*N-[1-(4-Cyanobenzyl)-5-imidazolemethyl] amino-4-  
(phenoxy) benzene*

*N-(4-Imidazolemethyl) amino-3-[(3-carboxyphenyl)oxy] benzene*

*1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl) -N-(4-  
cyanobenzyl) amino] -4-(phenoxy) benzene*

*(±)-4-[(4-imidazolylmethyl) amino] pentyl-1-(phenoxy) benzene*

*1-[(N-(1-(4-cyanobenzyl)-5-imidazolylmethyl) -N-(n-  
butyl) amino) methyl] -4-(phenoxy) benzene*

*4-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl) -N-(n-butyl) amino] -  
1-(phenylthio) benzene*

Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 16

(±)-4-[N-(1-(4-cyanobenzyl)-4-imidazolylmethyl)-N-(n-butyl)amino]-1-(phenylsulfinyl)benzene

3-[N-(4-imidazolylmethyl)-N-(n-butyl)amino]-N-(phenyl)benzenesulfonamide and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

4-{3-[4-(-2-Oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[4-3-Methyl-2-oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[4-(-2-Oxo-piperidin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[3-Methyl-4-(2-oxopiperidin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[4-(2-Oxo-pyrrolidin-1-yl)-benzyl]-3H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[4-(3-Methyl-2-oxo-2-H-pyrazin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[2-Methoxy-4-(2-oxo-2-H-pyridin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{1-[4-(5-Chloro-2-oxo-2H-pyridin-1-yl)-benzyl]-1H-pyrrol-2-ylmethyl}-benzonitrile

4-[1-(2-Oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

4-[3-(2-Oxo-1-phenyl-1,2-dihydropyridin-4-ylmethyl)-3H-imidazol-4-ylmethyl]benzonitrile

Applicants : N. Rosen et al.  
 U.S. Serial No. : 09/445,054  
 Filing Date : March 27, 2000  
 Page : 17

4-{3-[1-(3-Chloro-phenyl)-2-oxo-1,2-dihydropyridin-4-ylmethyl]-3H-imidazol-4-ylmethyl}benzonitrile

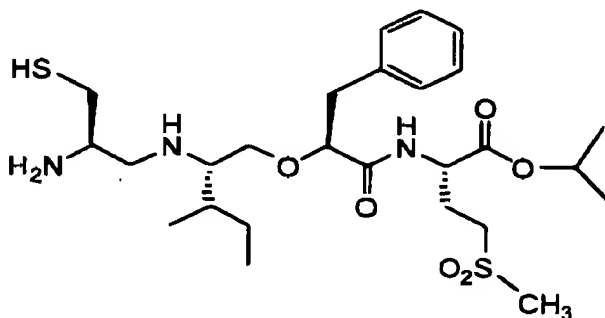
or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

55. (New) The method according to Claim 49 wherein the prenyl-protein transferase inhibitor is selected from:

2(S) - [2(S) - [2(R) -Amino-3-mercapto] -propylamino-

3(S) -methyl] -pentyloxy-3-phenylpropionyl-methionine sulfone

isopropyl ester. (Compound A)



1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

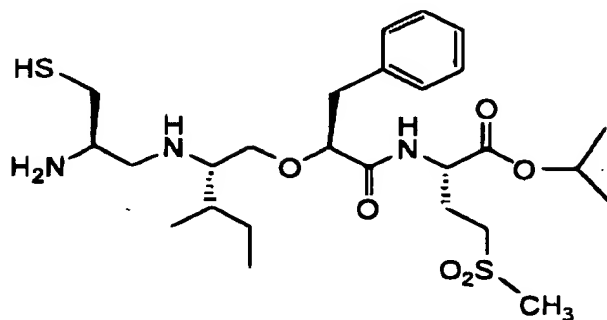
(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.



Applicants : N. Rosen et al.  
U.S. Serial No. : 09/445,054  
Filing Date : March 27, 2000  
Page : 18



56. (New) A pharmaceutical composition comprising an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent which is a microtubule-stabilizing agent, the composition which achieves a synergistic effect for treating cancer in a mammal in need thereof.

57. (New) A method of preparing a pharmaceutical composition which comprises mixing an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent which is a microtubule-stabilizing agent, said composition capable of achieving a synergistic effect for treating cancer in a mammal.